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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,121	12/06/2001	Ingrid W. Caras	GENENT.046DV1	3508

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
NICHOLS, CHRISTOPHER J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,121	CARAS, INGRID W.	
	Examiner	Art Unit	
	Christopher J Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35 and 40-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35 and 40-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4.3.02*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *8.2.04*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Response and Amendment filed 26 August 2004 have been received and entered in full.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

3. The Objection to the Specification as set forth at pp. 2 ¶4 in the previous Office Action (26 May 2004) is hereby *withdrawn* in view of Applicant's amendments (26 August 2004).

Maintained Objections And/Or Rejections

4. Claims **35** and **40-49** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons as set forth at pp. 2 ¶4 in the previous Office Action (26 May 2004).

5. Applicant traversed the rejection of the claims on the following grounds: **(a)** SEQ ID NO: 2 and 4 are known as AL-2, EFL-6, and ephrin-B3 in the art and have known activity, **(b)** the references Pasquale (1997) "The Eph Family of Receptors." Curr. Opin. Cell Biol. **9**(5): 608-615 and Gale & Yancopoulos (1999) "Growth factors acting via endothelial cell-specific receptor tyrosine kinases: VEGFs, Angiopoietins, and ephrins in vascular development." Genes &

Development **13**: 1055-1066 support vascularization activity for ephrins, and **(c)** the skilled artisan has sufficient guidance to make the claimed derivatives of SEQ ID NO: 2 and 4.

6. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

7. On "**(a)**", the Examiner accepts the argument and evidence presented in the Response and Exhibits that the instantly claimed polypeptides (SEQ ID NO: 2 and 4) are known as AL-2, EFL-6, and currently ephrin-B3 in the art. The art teaches the EphB3 the receptor of ephrin-B3 (also known as AL-2 ad EFL-6 according to Applicant pp. 8 of Response filed 26 August 2004) are involved in nervous system guidance. For instance, Cheng *et al.* "The ephrins and Eph receptor in angiogenesis." Cytokine & Growth Factor Reviews **13**: 75-85 teaches that knock-out mice of EphB3 -/- show no vascular defects but defects in the corpus collosum (the area between the hemispheres where nerve tracts cross) (Table 1). In addition, Yu *et al.* (21 November 2003) "Mouse EphrinB3 Augments T-cell Signaling and Responses to T-cell Receptor Ligation." J Biol Chem. **278**(47): 47209-16 teach that ephrin-B3 receptors are expressed on peripheral T cells and monocytes/macrophages. Yu *et al.* teaches that ephrin-B3 plays an important role in T-cell/T-cell and T-cell/antigen-presenting cell collaboration to enhance T-cell activation and function. Thus none of the above references teach that ephrin-B3 (herein claimed as AL-2 represented by SEQ ID NO: 2 and SEQ ID NO: 4) play any role in vascularization (Figures 3-5).

8. On "**(b)**", Pasquale (1997) and Gale & Yancopoulos (1999) teach that ephrinB2 and Eph receptors are involved in vascularization. However, neither provides any support for ephrin-B3, the instantly claimed ephrin, to be involved in vascularization.

9. On "**(c)**", no such evidence is present in the Specification or the prior art to support the claims. And in light of the complexity of the claims goals, the skilled artisan is not reasonably instructed as to which, if any, rate determining steps of neovascularization variants, homologues, analogues, orthologues, fragments, muteins, isoforms which are encompassed by AL-2 polypeptides which share 95% or greater sequence homology to the amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4 are involved in to a degree which is considered effective. Also, no evidence is present that any one or all of the variants, homologues, analogues, orthologues, fragments, muteins, isoforms which are encompassed by AL-2 polypeptides which share 95% or greater sequence homology to the amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4 will have any effect on neovascularization thus presenting an invitation to experiment. Firstly, to determine which steps any or all of the variants, homologues, analogues, orthologues, fragments, muteins, isoforms which are encompassed by AL-2 polypeptides which share 95% or greater sequence homology to the amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4 are involved in and then which of the multitude of variants, homologues, analogues, orthologues, fragments, muteins, isoforms which are encompassed by AL-2 polypeptides which share 95% or greater sequence homology to the amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4 have a desired effect.

10. Claims **35** and **40-49** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention for the reasons as set forth at pp. 9-10 ¶16-21 in the previous Office Action (26 May 2004).

11. Applicant traversed the rejection of the claims on the following grounds: **(a)** the Specification contains extensive teaching for making and using the variants claimed and **(b)** written description can be satisfied by a combination of structural and functional features

12. Applicant's arguments have been taken into consideration and are not found persuasive for the following reasons.

13. On "**(a)**", while ephrin-B3 and variants thereof which have vascularization activity may constitute a fecund ground for investigation, the CAFC ruled in *Genentech Inc. v. Novo Nordisk A/S* (CA FC) **42 USPQ2d 1001** (1997) that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Citing *Brenner v. Manson,* **383 U.S. 519, 536, 148 USPQ 689, 696** (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). Therefore the CFAC stated that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. That requirement has not been met in the instant specification with respect to ephrin-B3 and variants thereof which have vascularization activity (as noted above ephrin-B3 is not shown or taught to have vascularization activity unlike eprin-B2).

14. On "**(b)**", the claims as instantly presented contain only structural but not explicit function parameters for the claimed variants.

Summary

15. No claims are allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

17. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN
October 21, 2004

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER